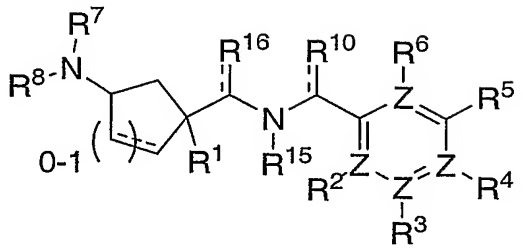
WHAT IS CLAIMED:

1. A compound of Formula I:



I

wherein:

Z is N or C, where no more than two Z are N;

R^1 is selected from: -C_{1-6}alkyl, -C_{0-6}alkyl-O-C_{1-6}alkyl, -C_{0-6}alkyl-S-C_{1-6}alkyl, -C_{0-6}alkyl-SO_2-C_{1-6}alkyl, -C_{0-6}alkyl-SO-C_{1-6}alkyl, -C_{0-6}alkyl-SO_2-NR^{12}-C_{0-6}alkyl, -(C_{0-6}alkyl)-(C_{3-7}cycloalkyl)-(C_{0-6}alkyl), hydroxy, heterocycle, -CN, -$NR^{12}R^{12}$, -$NR^{12}COR^{13}$, -$NR^{12}SO_2R^{14}$, -COR^{11}, -$CONR^{12}R^{12}$, and phenyl;, where alkyl and the cycloalkyl are unsubstituted or substituted with 1-7 substituents independently selected from: halo, hydroxy, -O-C_{1-3}alkyl, trifluoromethyl, C_{1-3}alkyl, -O-C_{1-3}alkyl, -COR^{11}, -SO_2R^{14}, -$NHCOR^{15}$, -$NHSO_2CH_3$, -heterocycle, =O, and -CN, and where phenyl and heterocycle are independently unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, trifluoromethyl and $NHCOR^{15}$;

when the Z attached to R^2 is N, R^2 is oxygen or is absent, and when the Z attached to R^2 is C, R^2 is selected from: hydrogen, C_{1-3}alkyl optionally substituted with 1-3 fluoro, -O-C_{1-3}alkyl optionally substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo and phenyl;

when the Z attached to R^3 is N, R^3 is oxygen or is absent, and when the Z attached to R^3 is C, R^3 is selected from: hydrogen, hydroxy, halo, C_{1-3}alkyl where the alkyl is unsubstituted or substituted with 1-6 substituents independently selected from: fluoro, hydroxy and $-COR^{11}$, $-NR^{12}R^{12}$, $-COR^{11}$, $-CONR^{12}R^{12}$, $-NR^{12}COR^{13}$, $-OCONR^{12}R^{12}$, $-NR^{12}CONR^{12}R^{12}$, -heterocycle, -CN, $-NR^{12}-SO_2-NR^{12}R^{12}$, $-NR^{12}-SO_2-R^{14}$, $-SO_2-NR^{12}R^{12}$ and nitro;

when the Z attached to R^4 is N, R^4 is oxygen or is absent, and when the Z attached to R^4 is C, R^4 is selected from: hydrogen, C_{1-3}alkyl optionally substituted with 1-3 fluoro, $-O-C_{1-3}$alkyl optionally substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo and phenyl;

R^5 is selected from: C_{1-6}alkyl where alkyl is unsubstituted or substituted with 1-6 substituents selected from fluoro and hydroxyl, $-O-C_{1-6}$alkyl where alkyl is unsubstituted or substituted with 1-6 fluoro, $-CO-C_{1-6}$alkyl where alkyl is unsubstituted or substituted with 1-6 fluoro, $-S-C_{1-6}$alkyl where alkyl is unsubstituted or substituted with 1-6 fluoro, pyridyl which is unsubstituted or substituted with one or more substituents selected from: halo, trifluoromethyl, C_{1-4}alkyl, and COR^{11}, fluoro, chloro, bromo, $-C_{4-6}$cycloalkyl, $-O-C_{4-6}$cycloalkyl, phenyl which is unsubstituted or substituted with one or more substituents selected from halo, trifluoromethyl, C_{1-4}alkyl, and COR^{11}, -O-phenyl which is unsubstituted or substituted with one or more substituents selected from: halo, trifluoromethyl, C_{1-4}alkyl, and COR^{11}, $-C_{3-6}$cycloalkyl where alkyl is unsubstituted or substituted with 1-6 fluoro, $-O-C_{3-6}$cycloalkyl where alkyl is unsubstituted or substituted with 1-6 fluoro, -heterocycle, -CN and $-COR^{11}$;

when the Z attached to R^6 is N, R^6 is oxygen or is absent, and when the Z attached to R^6 is C, R^6 is selected from: hydrogen, C_{1-3}alkyl optionally substituted with 1-3 fluoro, $-O-C_{1-3}$alkyl optionally substituted with 1-3 fluoro, hydroxy, chloro, fluoro, bromo and phenyl;

R^7 is selected from: hydrogen, C_{1-8}alkyl which is unsubstituted or substituted with 1-6 substituents selected from: hydroxy, halo, $-O-C_{1-6}$alkyl, CN, $-NR^{12}R^{12}$, $-NR^{12}COR^{13}$, -

$NR^{12}SO_2R^{14}$, $-COR^{11}$, $-CONR^{12}R^{12}$, phenyl and heterocycle, where the alkyl, phenyl, and heterocycle are unsubstituted or substituted with 1-3 substituents selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, $-CO_2H$, $-CO_2-C_{1-6}$alkyl, and trifluoromethyl, and $-SO_2C_{1-6}$alkyl which is unsubstituted or substituted with 1-6 substituents selected from: hydroxy, halo, $-O-C_{1-6}$alkyl, CN, $-NR^{12}R^{12}$, $-NR^{12}COR^{13}$, $-NR^{12}SO_2R^{14}$, $-COR^{11}$, $-CONR^{12}R^{12}$, phenyl and heterocycle, where the alkyl, phenyl, and heterocycle are unsubstituted or substituted with 1-3 substituents selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, $-CO_2H$, $-CO_2-C_{1-6}$alkyl, and trifluoromethyl; R^8 is selected from C_{1-10}alkyl, $-SO_2C_{1-10}$alkyl, pyridyl or phenyl, unsubstituted or substituted with 1-5 substituents selected from: hydroxy, halo, $-O-C_{1-6}$alkyl, $-S-C_{1-6}$alkyl, CN, $-NR^{12}R^{12}$, $-NR^{12}COR^{13}$, $-NR^{12}SO_2R^{14}$, $-COR^{11}$, $-CONR^{12}R^{12}$, $-SO_2R^{14}$, heterocycle , =O (where the oxygen is connected via a double bond), phenoxy and phenyl, where the alkyl, phenyl, phenoxy and heterocycle are unsubstituted or substituted with 1-3 substituents selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, $-COR^{11}$, -CN, $-NR^{12}R^{12}$, $-SO_2R^{14}$, $-NR^{12}COR^{13}$, $-NR^{12}SO_2R^{14}$, and $-CONR^{12}R^{12}$, where the alkyl and alkoxy are optionally substituted with 1-5 fluoro;

R^{10} and R^{16} are independently selected from: =O, hydrogen, phenyl, C_{1-6}alkyl which is unsubstituted or substituted with 1-6 of the following substituents: $-COR^{11}$, hydroxy, fluoro, chloro, and $-O-C_{1-3}$alkyl; and,

R^{11} is independently selected from: hydroxy, hydrogen, C_{1-6} alkyl, $-O-C_{1-6}$alkyl, benzyl, phenyl, C_{3-6} cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, $-CO_2H$, $-CO_2-C_{1-6}$ alkyl, and trifluoromethyl,

R^{12} is selected from: hydrogen, C_{1-6} alkyl, benzyl, phenyl, C_{3-6} cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, $-CO_2H$, $-CO_2-C_{1-6}$alkyl, and trifluoromethyl, and

R^{13} is selected from: hydrogen, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl, C_{3-6} cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6}alkyl, and trifluoromethyl,

R^{14} is selected from: hydroxy, C_{1-6} alkyl, -O-C_{1-6}alkyl, benzyl, phenyl, C_{3-6} cycloalkyl, where the alkyl, phenyl, benzyl, and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents independently selected from: halo, hydroxy, C_{1-3}alkyl, C_{1-3}alkoxy, -CO_2H, -CO_2-C_{1-6}alkyl, and trifluoromethyl,

R^{15} is selected from hydrogen and C1-3alkyl;

or, R^2 and R^{15} are joined together to form a carbocycle or heterocycle ring with a linker selected from: -$CH_2(CR^{17}R^{17})_{1-3}$-, -$CH_2NR^{18}$-, -$NR^{18}$-$CR^{17}R^{17}$-, -$CR^{17}R^{17}O$-, -$CR^{17}R^{17}SO_2$-, -$CR^{17}R^{17}SO$-, -$CR^{17}R^{17}S$-, -$CR^{17}R^{17}$-, and -$NR^{18}$- (with the left side of the linker being bonded to the amide nitrogen at R^{15}),

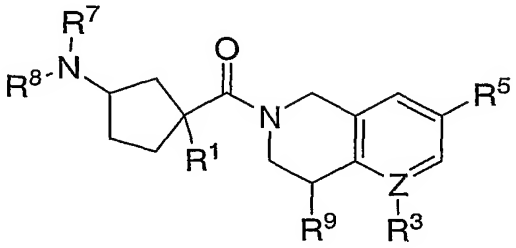
R^{17} is selected from: hydrogen, hydroxy, halo and C_{1-3}alkyl, where the alkyl is unsubstituted or substituted with 1-6 substituents independently selected from: fluoro, and hydroxy, -$NR^{12}R^{12}$, -COR^{11}, -$CONR^{12}R^{12}$, -$NR^{12}COR^{13}$, -$OCONR^{12}R^{12}$, -$NR^{12}CONR^{12}R^{12}$, -heterocycle, -CN, -NR^{12}-SO_2-$NR^{12}R^{12}$, -NR^{12}-SO_2-R^{14}, -SO_2-$NR^{12}R^{12}$, and =O, and where when one R^{17} is connected to the ring via a double bond the other R^{17} at the same position is absent,

R^{18} is selected from: hydrogen, C_{1-3}alkyl unsubstituted or substituted with 1-6 substituents independently selected from: fluoro, and hydroxy, COR^{13}, SO_2R^{14}, and $SO_2NR^{12}R^{12}$;

the dashed line represents an optional bond;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

2. The compound of claim 1 of the formula Ia:

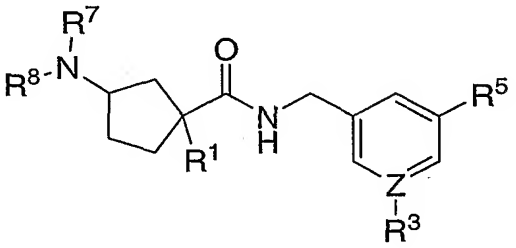


Ia

wherein R^9 is selected from: hydrogen, hydroxy, C_{1-3}alkyl unsubstituted or substituted with 1-6 substituents independently selected from fluoro and hydroxy, -COR^{11}, -$CONR^{12}R^{12}$, -$NR^{12}COR^{11}$, -NR^{12}-SO_2-R^{14}, -SO_2-$NR^{12}R^{12}$, and =O, where R^9 is connected to the ring via a double bond,

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

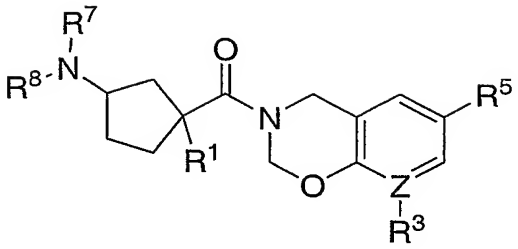
3. The compound of claim 1 of the formula Ib:



Ib

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

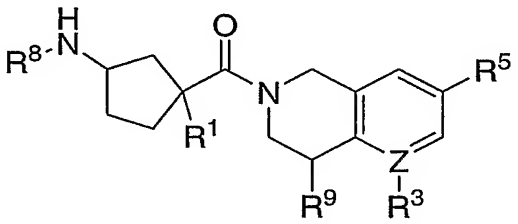
4. The compound of claim 1 of the formula Ic:



Ic

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

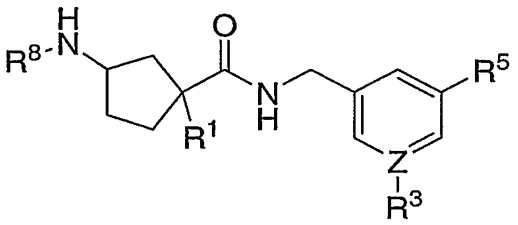
5. The compound of claim 1 of the formula Id:



Id

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

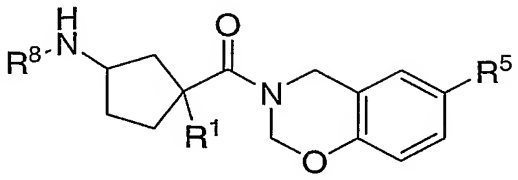
6. The compound of claim 1 of the formula Ie:



Ie

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

7. The compound of claim 1 of the formula If:



If

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

8. The compound of claim 1 wherein R^1 is selected from:

$-C_{1-6}$alkyl, $-C_{0-6}$alkyl-O-C_{1-6}alkyl, and -(C_{0-6}alkyl)-(C_{3-7}cycloalkyl)-(C_{0-6}alkyl), where the alkyl and the cycloalkyl are unsubstituted or substituted with 1-7 substituents independently selected from: halo, hydroxy, -O-C_{1-3}alkyl, trifluoromethyl, C_{1-3}alkyl, -O-C_{1-3}alkyl, $-COR^{11}$, -CN, $-NR^{12}R^{12}$, and $-CONR^{12}R^{12}$,

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

9. The compound of claim 1 wherein R^1 is selected from:

$-C_{1-6}$alkyl unsubstituted or substituted with 1-6 substituents independently selected from: halo, hydroxy, -O-C_{1-3}alkyl, trifluoromethyl, and $-COR^{11}$,

$-C_{0-6}$alkyl-O-C_{1-6}alkyl- unsubstituted or substituted with 1-6 substituents independently selected from: halo, trifluoromethyl, and $-COR^{11}$,

-(C_{3-5}cycloalkyl)-(C_{0-6}alkyl) unsubstituted or substituted with 1-7 substituents independently selected from: halo, hydroxy, -O-C_{1-3}alkyl, trifluoromethyl, and -COR^{11},

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

10. The compound of claim 1 wherein R^1 is C_{1-6}alkyl unsubstituted or substituted with 1-6 substituents selected from hydroxyl and fluoro, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

11. The compound of claim 1 wherein R^1 is selected from: -$CH(CH_3)_2$, -$CH(OH)CH_3$ and -CH_2CF_3, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

12. The compound of claim 1 wherein R^1 is selected from: thiazolyl, unsubstituted or substituted with $NHCOR^{15}$, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

13. The compound of claim 1 wherein the Z attached to R^2 is C, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

14. The compound of claim 1 wherein R^2 is hydrogen or R^2 and R^{15} are linked by -CH_2-CH_2- or -CH_2-O-, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

15. The compound of claim 1 wherein when the Z attached to R^3 is N, R^3 is absent or is or O, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

16. The compound of claim 1 wherein when the Z attached to R^3 is N, R^3 is absent. and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

17. The compound of claim 1 wherein when the Z attached to R^3 is C, R^3 is selected from: hydrogen, halo, hydroxy, C_{1-3}alkyl, where the alkyl is unsubstituted or substituted with 1-6 substituents independently selected from: fluoro, and hydroxy, -COR^{11}, -$CONR^{12}R^{12}$, -heterocycle, -NR^{12}-SO_2-$NR^{12}R^{12}$, -NR^{12}-SO_2-R^{14}, -SO_2-$NR^{12}R^{12}$, -nitro, and -$NR^{12}R^{12}$;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

18. The compound of claim 1 wherein when the Z attached to R^3 is C R^3 is hydrogen, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

19. The compound of claim 1 wherein the Z attached to R^4 is C, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

20. The compound of claim 1 wherein R^4 is hydrogen, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

21. The compound of claim 1 wherein R^5 is selected from: C_{1-6}alkyl substituted with 1-6 fluoro, -O-C_{1-6}alkyl substituted with 1-6 fluoro, chloro, bromo, and phenyl, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

22. The compound of claim 1 wherein R^5 is selected from: trifluoromethyl, trifluoromethoxy, chloro, bromo, and phenyl, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

23. The compound of claim 1 wherein R^5 is trifluoromethyl, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

24. The compound of claim 1 wherein the Z attached to R^6 is C, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

25. The compound of claim 1 wherein R^6 is hydrogen, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

26. The compound of claim 1 wherein R^7 is hydrogen or methyl and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

27. The compound of claim 1 wherein R^7 is hydrogen, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

28. The compound of claim 1 wherein R^8 is selected from: C_{1-8}alkyl optionally substituted with hydroxy, C_{1-6}alkyl substituted with 1-6 fluoro, C_{1-6}alkyl substituted with $-COR^{11}$, benzyl, unsubstituted or substituted with 1-3 substituents selected from: hydroxy, methoxy, chloro, fluoro, $-COR^{11}$, methyl and trifluoromethyl, $-CH_2$-pyridyl, unsubstituted or substituted with 1-3 substituents selected from: hydroxy, methoxy, chloro, fluoro, methyl and trifluoromethyl, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

29. The compound of claim 1 wherein R^9 is hydroxy, hydrogen, =O, where R^9 is connected to the ring via a double bond, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

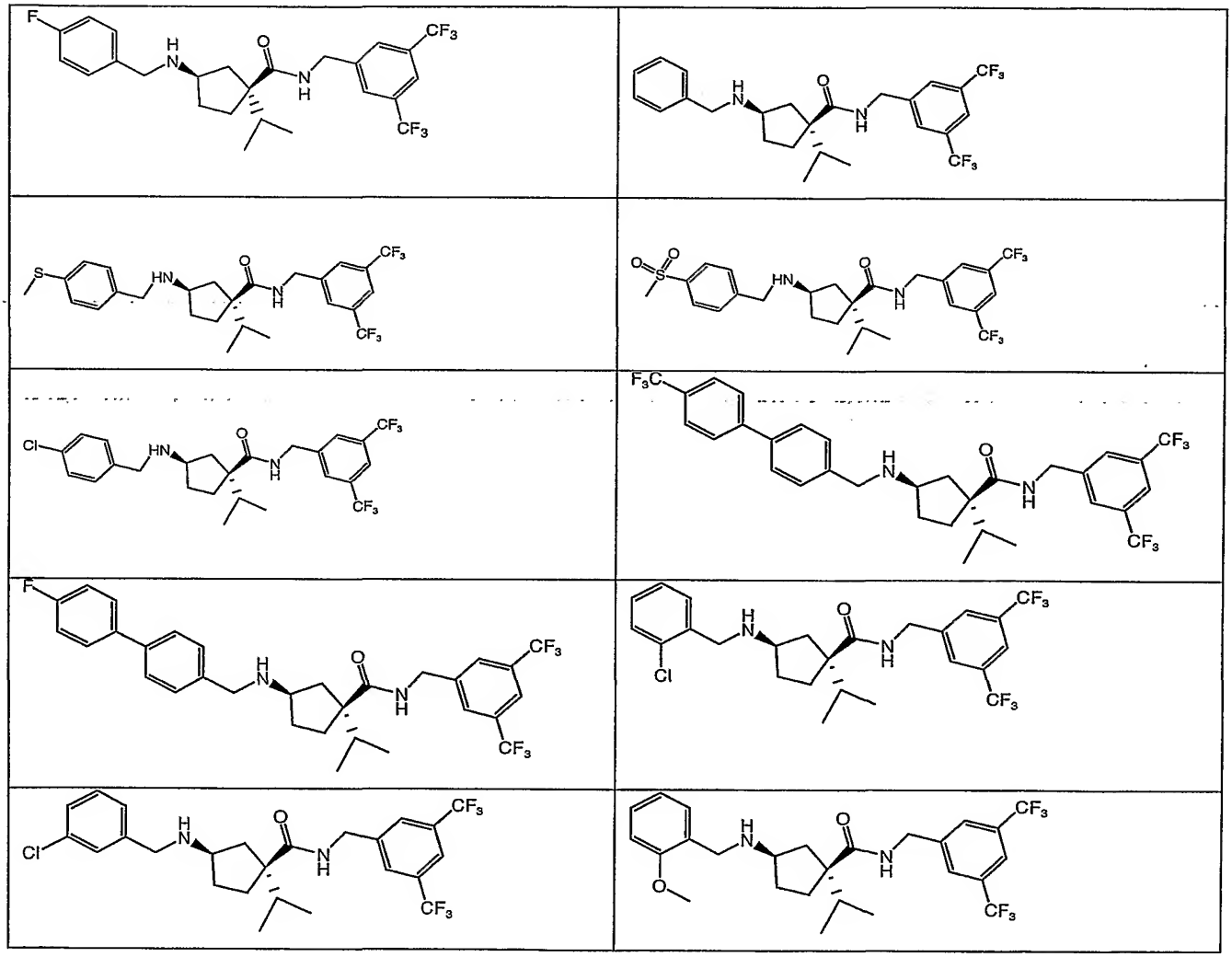
30. The compound of claim 1 wherein R^9 is hydrogen, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

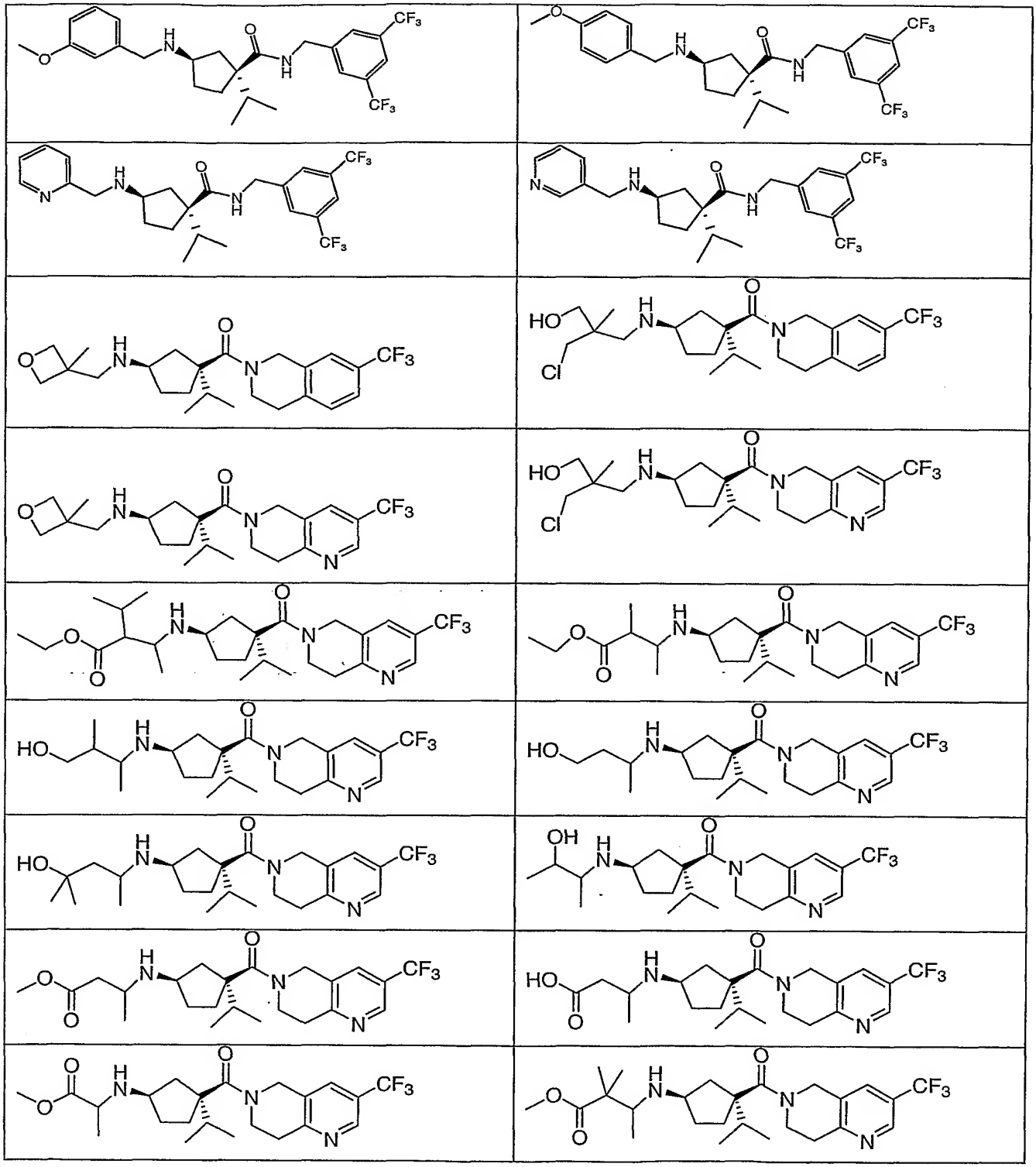
31. The compound of claim 1 wherein R^{10} is hydrogen and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

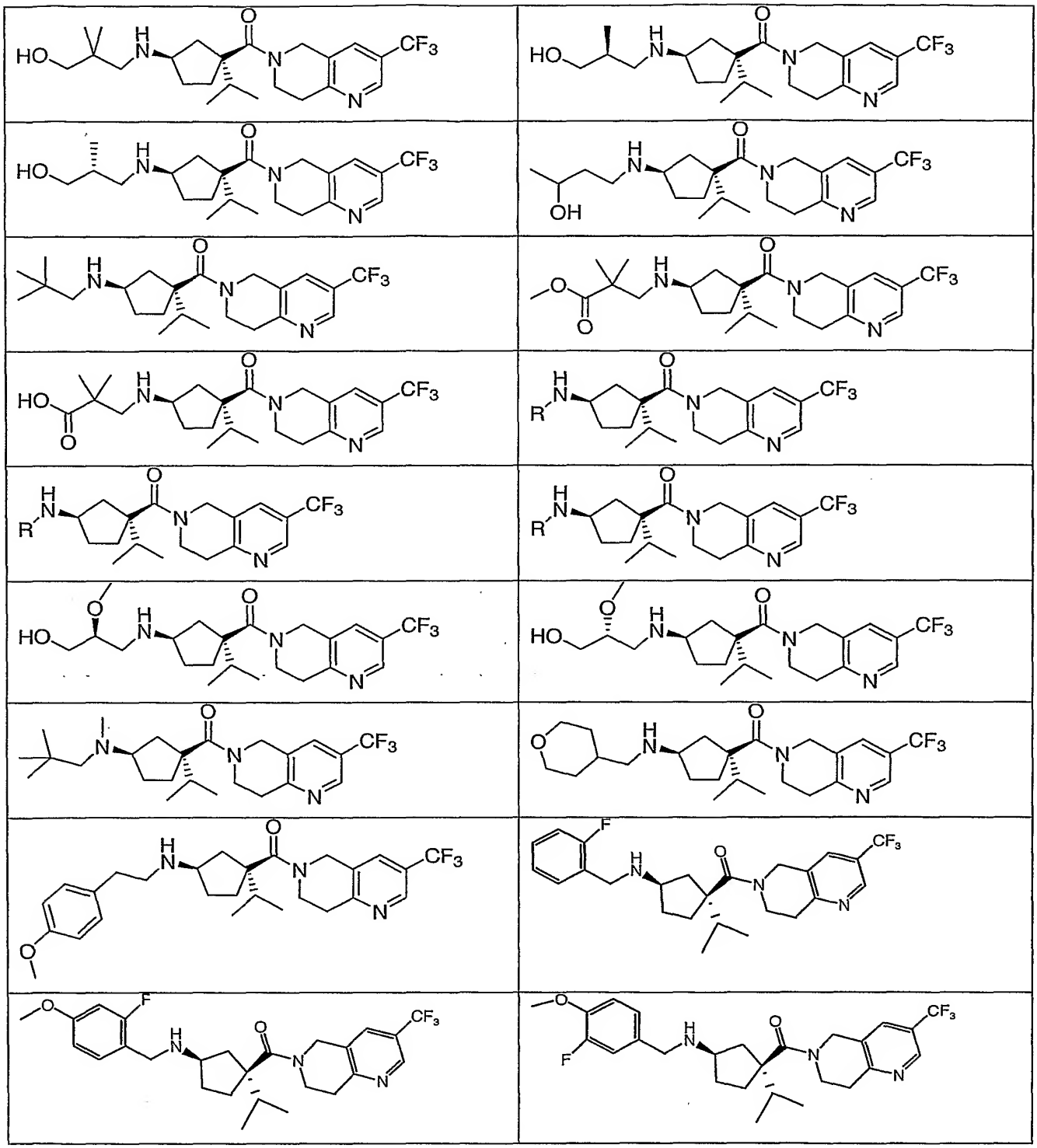
32. The compound of claim 1 wherein R^{15} is hydrogen or is joined to R^2, and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

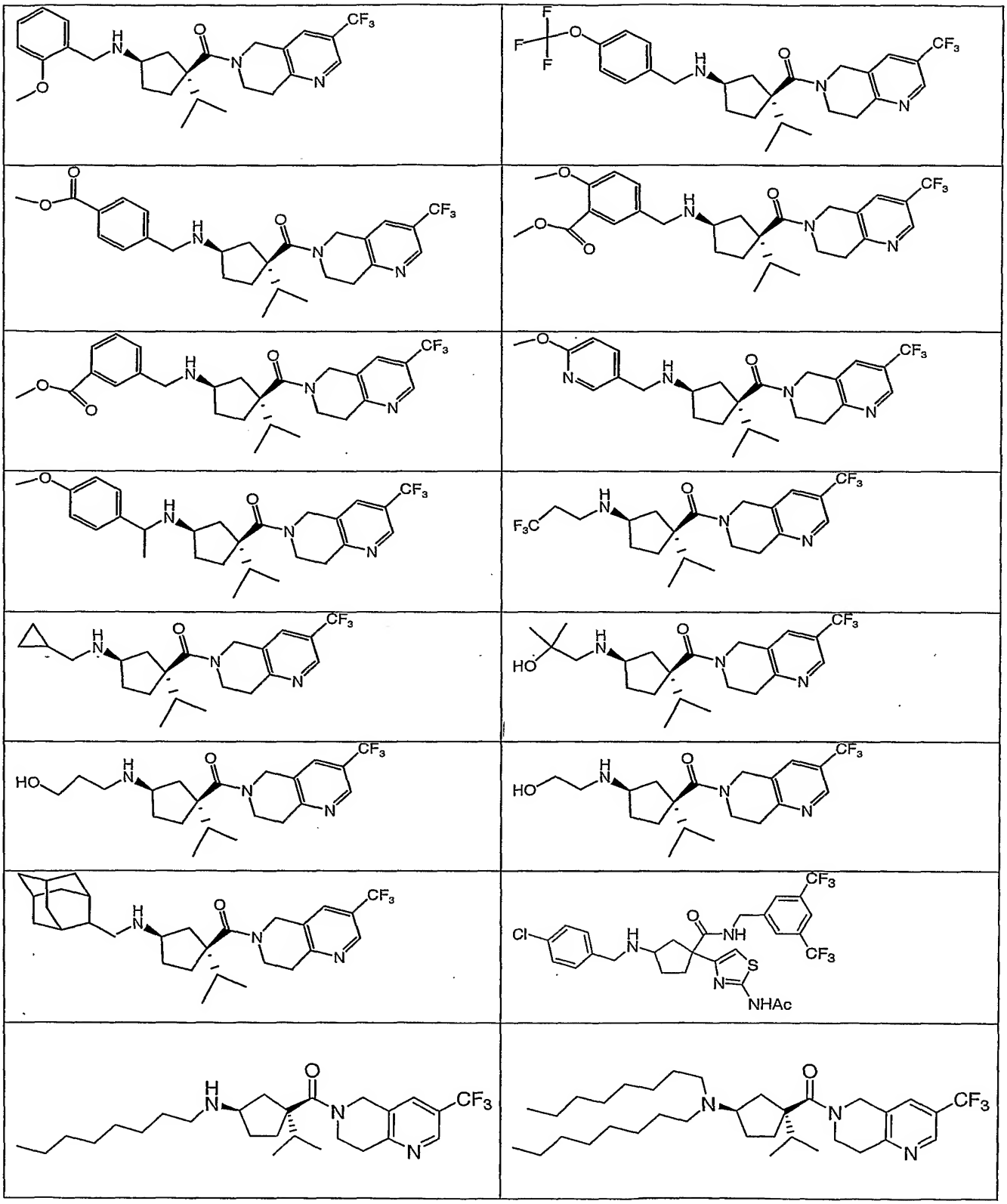
33. The compound of claim 1 wherein R^{16} is and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

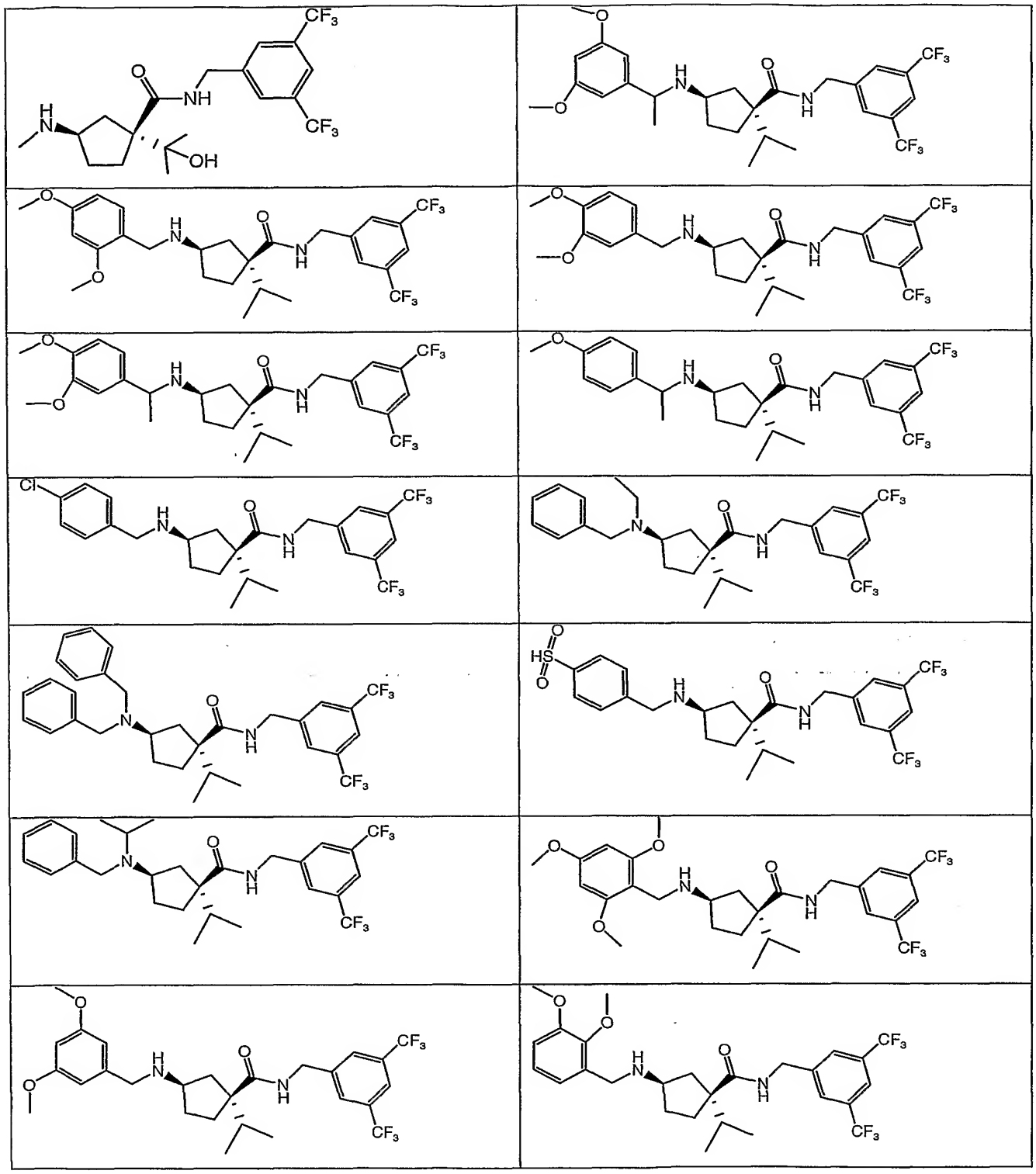
34. A compound selected from:

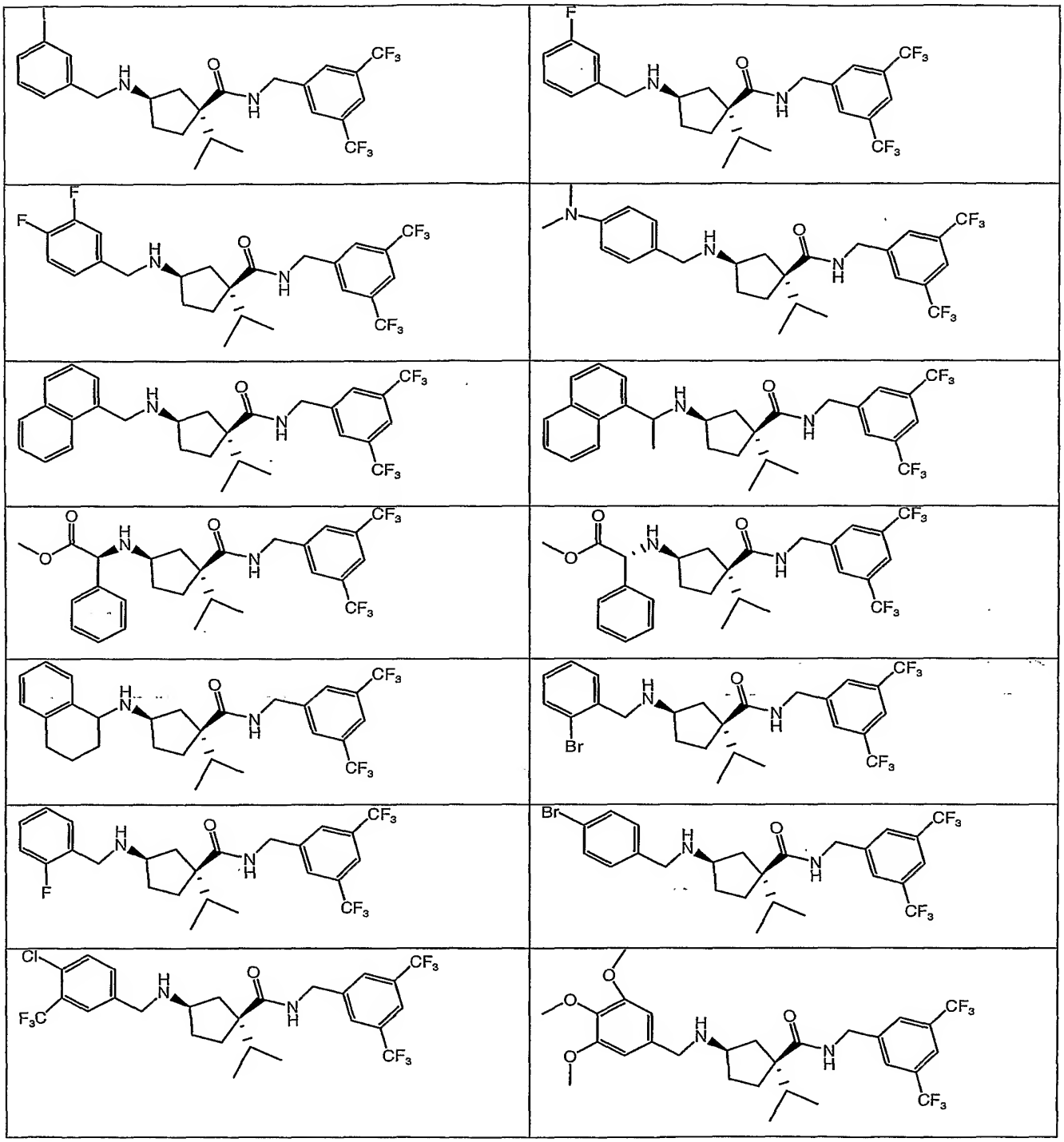


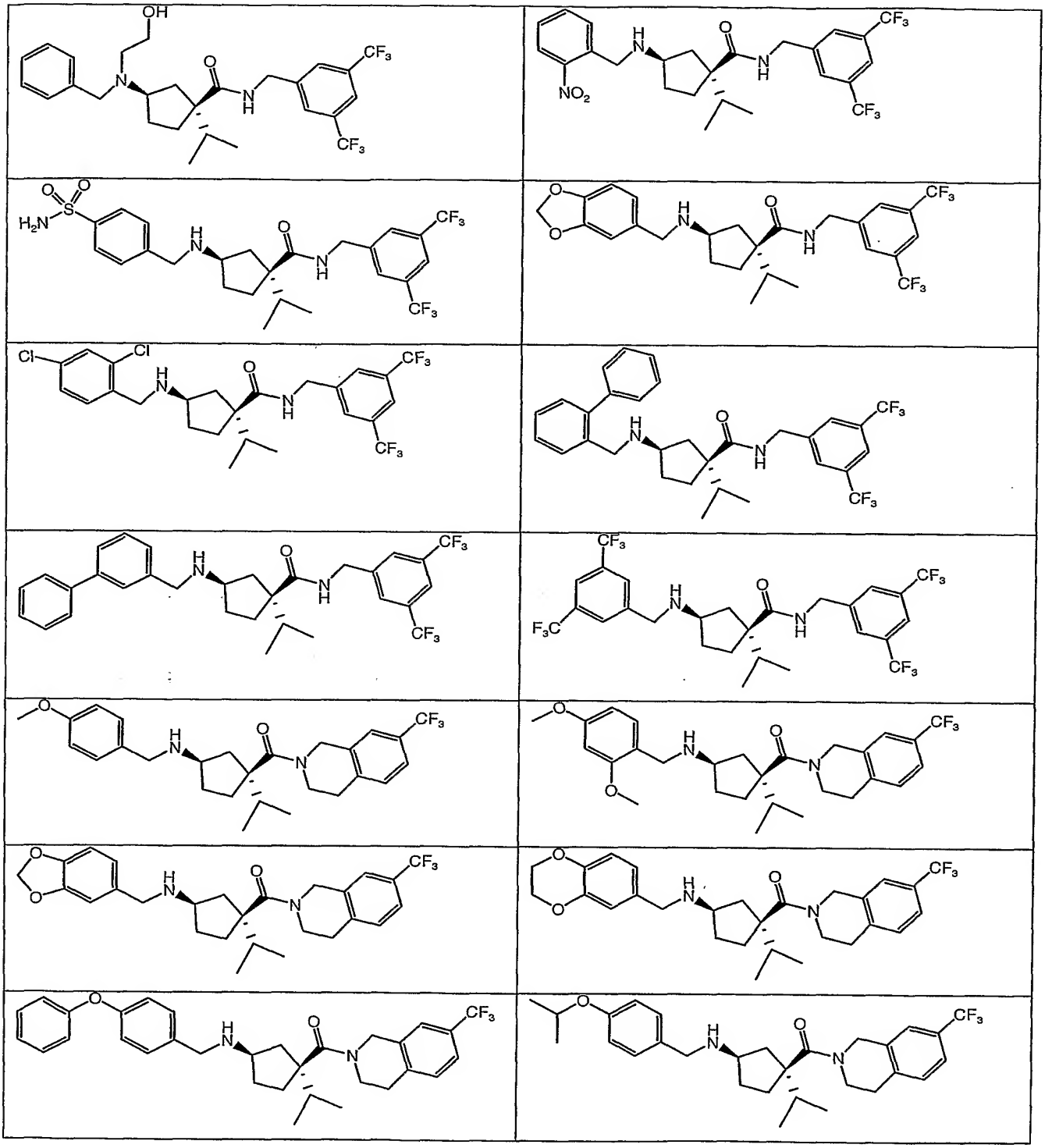


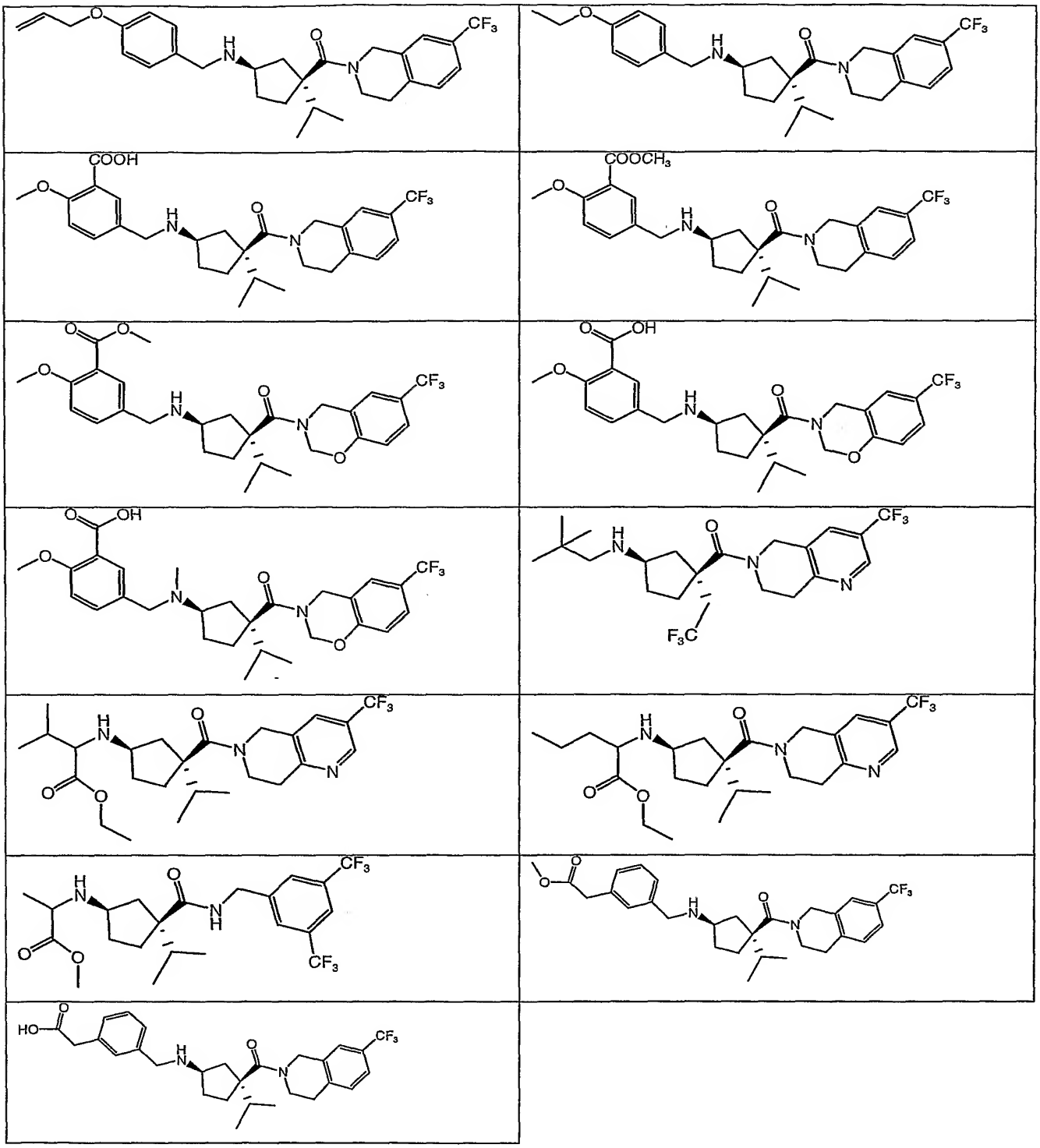












and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

35. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.

36. A method for modulations of chemokine receptor activity in a mammal which comprises the administration of an effective amount of a compound of Claim 1.

37. A method for treating, ameliorating, controlling or reducing the risk of an inflammatory and immunoregulatory disorder or disease which comprises the administration to a patient of an effective amount of a compound of Claim 1.

38. A method for treating, ameliorating, controlling or reducing the risk of rheumatoid arthritis which comprises the administration to a patient of an effective amount of a compound of Claim 1.